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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/714,692
Filing Date: November 16, 2000
Appellant(s): LEE ET AL.

Benjamin Aaron Adler
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 18 October 2004 (hereinafter, the Brief).

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 20-23 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Villalona-Calero et al. "A phase I trial of human corticotropin-releasing factor (hCRF) in patients with peritumoral brain edema" Annals of Oncology, vol 9, (1998), pp 71-77.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Villalona-Calero et al. (Ann Oncol 9: 71-77, 1998).

Villalona-Calero et al. teach administering a corticotropin releasing factor 2 (CRFR2) agonist, specifically human corticotropin releasing factor (CRF), to a target tissue. Villalona-Calero et al. teach that patients with primary or secondary brain tumors with evidence of edema are administered CRF intravenously, by continuous infusion (pg 72, col 1, first and second full paragraphs). Villalona-Calero et al. disclose that hCRF reduces water content in tumor and peritumoral tissue in brain tumor models *in vivo* when administered subcutaneously (pg 72, col 1; pg 76, first paragraph). Villalona-Calero et al. also indicate that this effect is a direct action the tumor microvasculature (pg 76, first paragraph).

Additionally, since Villalona-Calero et al. administer human CRF, a CRFR2 agonist, to the same subject population and the same tissue as recited in the claims, inhibition of angiogenesis must have been inherently occurring in the prior art of Villalona-Calero et al. (see *Ex parte Novitski*, 26 USPQ2d 1389 (BPAI 1993); see also *Integra LifeSciences I Ltd. V. Merck KGaA*, (DC SCalif) 50 USPQ2d 1846).

(11) Response to Argument

Appellant argues at the bottom of pg 6 through the top of pg 7 of the Brief that the present invention is drawn to a method of using a corticotrophin releasing factor receptor 2 (CRFR2) agonist to inhibit angiogenesis in a target tissue. Appellant indicates that Villalona-Calero et al. teach a method of using human corticotrophin releasing factor (hCRF) to treat patients having peritumoral brain edema. Appellant asserts that Villalona-Calero et al. teach human CRF inhibits vascular leakage of plasma constituents in response to injury, but do not teach or suggest a method of using CRF to inhibit angiogenesis in a target tissue, as claimed (pg 7 of the Brief). As discussed above in the previous section, Villalona-Calero et al. teach that patients with primary or secondary brain tumors with evidence of edema are administered a CRFR2 agonist (human corticotropin-releasing factor (hCRF)) intravenously, by continuous infusion (pg 72, col 1, first and second full paragraphs). It is noted that edema is the swelling of an organ or tissue due to accumulation of excess fluid. Villalona-Calero et al. disclose that hCRF reduces water content in tumor and peritumoral tissue in brain tumor models *in vivo* when administered subcutaneously (pg 72, col 1; pg 76, first paragraph). Villalona-Calero et al. also indicate that this effect is a direct action on the tumor microvasculature (pg 76, first paragraph). However, since Villalona-Calero et al. administer human corticotrophin releasing factor (a CRFR2 agonist) to the same subject population and to the same tissue as recited in the claims, inhibition of angiogenesis must have been inherently occurring in the prior art of Villalona-Calero et al. (see *Ex parte Novitski*, 26 USPQ2d 1389 (BPAI 1993); see also *Integra LifeSciences I Ltd. V. Merck KGaA*, (DC SCalif) 50 USPQ2d 1846). The disclosure of Villalona-Calero et al. fully meets the terms of the claimed method because a CRFR2 agonist

(corticotropin releasing factor) inherently possesses angiogenesis-inhibiting activity. A compound and all of its properties are inseparable; they are one and the same thing and simply stating a new property of CRF does not render the claimed method of inhibiting angiogenesis of the instant application free of the art (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971); *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978)).

At pg 7 of the Brief, Appellant submits that Villalona-Calero et al. do not teach or suggest any scientific relationship between angiogenesis and the prevention of vascular leakage, and one of ordinary skill in the art would readily recognize that these are two distinct biological processes. Appellant also states that absent a teaching that shows any relationship between angiogenesis and anti-edematous effects, one of skill in the art would have no reasonable and logical scientific basis to recognize or suspect that human CRF inherently possesses angiogenesis-inhibiting activity. At the bottom of pg 7 and at top of pg 8 of the Brief, Appellant also contends that the Examiner's assertion that human CRF inherently possesses angiogenesis-inhibiting activity is not supported or suggested by any scientific reasoning or data. At the middle of pg 8 of the Brief, Appellant interprets the Examiner's reasoning of anticipation as "patenting of any new or novel method of using a compound is precluded once the prior art has described using the compound for whatever purpose in similar target tissues". Although Villalona-Calero et al. do not specifically teach a relationship between angiogenesis and vascular leakage, Villalona-Calero et al. disclose that human CRF inhibits vascular leakage of plasma constituents in response to injury and has a direct action on brain tumor microvasculature (pg 71, last two lines of col 2; pg 76, first paragraph). Furthermore, although the mechanism of action of

human CRF was not known at the time of filing of the instant application (Villalona-Calero et al., pg 76, col 2, second full paragraph), Villalona-Calero et al. administer human corticotrophin releasing factor (a CRFR2 agonist) to the same subject population and to the same tissue as required by the instant claims. Therefore, inhibition of angiogenesis must have been inherently occurring in the prior art of Villalona-Calero et al. (see *Ex parte Novitski*, 26 USPQ2d 1389 (BPAI 1993) ; see also *Integra LifeSciences I Ltd. V. Merck KGaA*, (DC SCalif) 50 USPQ2d 1846). The broad method steps claimed in the instant application are the same as the steps disclosed in Villalona-Calero et al. Appellant's assertion that CRFR2 agonists, such as human CRF, inhibit angiogenesis in a target tissue was already inherent in Villalona-Calero et al. If Villalona-Calero et al. would have attempted to measure the effect of human CRF on angiogenesis in brain tumor tissue, they would have uncovered it. Thus, Villalona-Calero et al. anticipate the claimed invention of the instant application. Furthermore, inherent anticipation does not require that one of ordinary skill in the art recognize an inherent feature in a prior art disclosure (*Schering Corp. v. Geneva Pharmaceuticals Inc.*, 67 USPQ2d 1664 (CAFC 2003); *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)).

It is noted that in the previous Office Actions of 04 March 2004 (pg 3) and 21 October 2003 (pg 3), the Examiner cited *Ex parte Novitski* and provided reasoning to support inherent anticipation of the claims. Furthermore, Appellant has misinterpreted the Examiner's basis for the instant anticipation rejection. The Examiner has not made any sweeping generalizations indicating that patenting of any new or novel method of using a compound is precluded once the prior art has described using the compound for whatever purpose in similar target tissues. In fact, the discovery of a new use for an old structure based on unknown properties of the structure

might be patentable to the discoverer as a process of using (see *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957). However, when the claim recites using an old composition or structure and the "use" is directed to a result or property of that composition or structure, then the claim is anticipated (see *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978). Regarding the instant application, since Villalona-Calero et al. teach the administration of human corticotrophin releasing factor (a CRFR2 agonist) to the same subject population and to the same tissue as recited in the claims, inhibition of angiogenesis must have been inherently occurring in the prior art. The disclosure of Villalona-Calero et al. fully meets the terms of the claimed method because a CRFR2 agonist (corticotropin releasing factor) inherently possesses angiogenesis-inhibiting activity. A compound and all of its properties are inseparable; they are one and the same thing and simply stating a new property of CRF does not render the claimed method of inhibiting angiogenesis of the instant application free of the art (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971); *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978)).

At the bottom of pg 8 through pg 9 and at the bottom of pg 10 of the Brief, Appellant asserts that the Examiner has failed to provide scientific rationale or legal evidence demonstrating inherency. Appellant states that the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. Appellant also contends that to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. It is noted that Appellant cites *Ex parte Levy*, 17 USPQ2d

1461 (Bd. Pat. App. & Inter. 1990), *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993), *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981), and *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) at pg 8-9 of the Brief for support. As discussed above, Villalona-Calero et al. do not specifically teach a relationship between angiogenesis and vascular leakage, but Villalona-Calero et al. disclose that human CRF inhibits vascular leakage of plasma constituents in response to injury and has a direct action on brain tumor microvasculature (pg 71, last two lines of col 2; pg 76, first paragraph). Although the mechanism of action of human CRF was not known at the time of filing of the instant application (Villalona-Calero et al., pg 76, col 2, second full paragraph), Villalona-Calero et al. administer human corticotrophin releasing factor (a CRFR2 agonist) to the same subject population and the same tissue as required by the instant claims. The broad method steps claimed in the instant application are the same as the steps disclosed in Villalona-Calero et al. Appellant's assertion that CRFR2 agonists, such as human CRF, inhibit angiogenesis in a target tissue was already inherent in Villalona-Calero et al. If Villalona-Calero et al. would have attempted to measure the effect of human CRF on angiogenesis in brain tumor tissue, they would have uncovered it (see *Ex parte Novitski*, 26 USPQ2d 1389 (BPAI 1993) ; see also *Integra LifeSciences I Ltd. V. Merck KGaA*, (DC SCalif) 50 USPQ2d 1846). As mentioned above, in the previous Office Actions of 04 March 2004 (pg 3) and 21 October 2003 (pg 3), the Examiner cited *Ex parte Novitski* and provided reasoning to support inherent anticipation of the claims. Inhibition of angiogenesis must have been inherently occurring in the prior art of Villalona-Calero et al. and thus, Villalona-Calero et al. anticipate the claimed invention of the instant application.

Furthermore, the fact patterns of the cases cited by the Appellant and of the instant rejection are significantly different, and the court decisions are not binding with regard to the instant rejections. For example, in *Ex parte Levy*, the Board of Patent Appeals and Interferences found that the reference applied under 35 U.S.C. § 102 did not disclose a biaxially oriented catheter balloon, as required by the claims of issue. The Board also determined that there was not enough basis to support the determination that the balloon taught in the reference was inherently biaxially oriented. Regarding *In re Robertson*, wherein the claim was drawn to a diaper with 3 fastening devices, the U.S. Court of Appeals Federal Circuit determined that the reference applied under 35 U.S.C. 102(e) only taught a diaper with 2 fastening devices and that the probability or possibility of the odd use of fasteners with other than their mates was insufficient to establish inherency. In *In re Rijckaert*, the U.S. Court of Appeals Federal Circuit reversed the obviousness rejection because inherency was based on what would result due to optimization of conditions and not what was necessarily present in the prior art. Finally, regarding *In re Oelrich*, the U.S. Court of Customs and Patent Appeals found that because the claim at issue required a means for generating a carrier frequency less than the minimum system resonant frequency, thereby necessitating a particular relationship between the carrier and the resonant frequencies, the required means was not inevitably present in the prior art system. In the instant application, although Villalona-Calero et al. do not specifically teach a relationship between angiogenesis and vascular leakage, Villalona-Calero et al. teach the administration of human corticotrophin releasing factor (a CRFR2 agonist) to the same subject population and to the same tissue as recited in the claims. Therefore, inhibition of angiogenesis (as required by the instant claims) must have been inherently occurring in the prior art. The disclosure of Villalona-

Calero et al. fully meets the terms of the claimed method because a CRFR2 agonist (corticotropin releasing factor) inherently possesses angiogenesis-inhibiting activity. Again, inherent anticipation does not require that one of ordinary skill in the art recognize an inherent feature in a prior art disclosure (*Schering Corp. v. Geneva Pharmaceuticals Inc.*, 67 USPQ2d 1664 (CAFC 2003); *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)).

At pg 10 of the Brief, Appellant asserts that the Examiner has not established that Villalona-Calero et al. anticipates the critical elements of the instant claims. However, Villalona-Calero et al. teach the administration of a corticotropin releasing factor 2 (CRFR2) agonist, specifically human corticotropin releasing factor (CRF), to a target tissue, as required by the instant claims. Villalona-Calero et al. also teach that patients with primary or secondary brain tumors with evidence of edema are administered CRF intravenously, by continuous infusion (pg 72, col 1, first and second full paragraphs), as required by the claims. Villalona-Calero et al. disclose that hCRF reduces water content in tumor and peritumoral tissue in brain tumor models *in vivo* when administered subcutaneously (pg 72, col 1; pg 76, first paragraph). Villalona-Calero et al. also indicate that this effect is a direct action the tumor microvasculature (pg 76, first paragraph). Since Villalona-Calero et al. administer human CRF, a CRFR2 agonist, to the same subject population and to the same tissue as recited in the claims, inhibition of angiogenesis must have been inherently occurring in the prior art of Villalona-Calero et al. The broad method steps claimed in the instant application are the same as the steps disclosed in Villalona-Calero et al. Appellant's assertion that CRFR2 agonists, such as human CRF, inhibit angiogenesis in a target tissue was already inherent in Villalona-Calero et al. If Villalona-Calero

et al. would have attempted to measure the effect of human CRF on angiogenesis in brain tumor tissue, they would have uncovered it. Therefore, Villalona-Calero et al. anticipate the claimed invention of the instant application.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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January 6, 2005

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